REMARKS

I. Status of the Claims

This response is deemed to put the case in condition for allowance or in better condition for appeal. Entry of this response is thus respectfully requested in accordance with 37 C.F.R. 1.116.

Claims 8-15 and 17-18 are currently pending, with claims 17 and 18 withdrawn from consideration as directed to a non-elected invention.

The Examiner has indicated that claims 11-15 are allowable.

II. Claim Rejections under 35 U.S.C. §112

The sole rejection that is outstanding is the rejection of claims 8-10 under 35 U.S.C. § 112, first paragraph. These claims are said to encompass subject matter that is not enabled by the specification. As described in greater detail below, Applicants respectfully disagree with the Office's conclusion for at least two general reasons: (i) the Office is applying an incorrect enablement standard, and (ii) the rationale presented in the Office Action is inconsistent with statements regarding enablement issues in the "Synopsis of Application of Written Description Guidelines" (Guidelines) promulgated by the Office.

With respect to the appropriate standard for enablement, the Office maintains the view that protein chemistry is highly unpredictable and cites several articles to support its conclusion that it would require undue experimentation to identify active variants of SEQ ID NOs:2, 4, 6, 8 and 10 because the effect of protein alterations "cannot be *predicted a priori* and must be determined empirically on a case-by-case basis " (Office Action at page 3, emphasis added). It thus appears that the Office is taking the position that variants cannot be claimed unless the specification provides sufficient guidance such that one of ordinary skill in the art can *predict a priori* what amino acid alterations can be made to SEQ ID NOs:2, 4, 6, 8, and 10 without altering the function of the native protein. Furthermore, the Office apparently considers the identification of active variants on an empirical basis to require undue experimentation. This

is not the correct standard for evaluating whether the enablement requirement is satisfied in this case.

As noted in earlier Office Actions, the Federal Circuit in its *In re Wands* decision (*In re Wands* 8 USPQ2d 1400, 858 F.2d 731, 737 (Fed. Cir. 1988)) provided guidance regarding what constitutes undue experimentation. In addition to the various *In re Wand* factors mentioned in earlier Office Actions, however, the court specifically addressed the issue of when considerable experimentation rises to the level of undue experimentation. As noted in the previous response, the court stated:

> [E]xperimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art...*The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.* (*In re Wands* 8 USPQ2d 1400, 858 F.2d 731, 737 (Fed. Cir. 1988) (emphasis added)).

This statement makes clear that the enablement requirement can be satisfied under certain circumstances, even if a "considerable" amount of experimentation is required to practice the invention. Thus, the ability to *predict a priori* which variants will be active is not required to satisfy the enablement requirement. The statement also supports the view that the enablement requirement can be satisfied by empirical determination of active variants under certain circumstances.

More specifically, as pointed out in the last response, this statement in the *In re Wands* decision indicates that experimentation is not deemed to be undue if EITHER of two requirements are satisfied: (1) the experimentation is routine, OR (2) the specification provides

reasonable guidance in the direction the experimentation should proceed. Although only *one* of these criteria need be satisfied, it is submitted that the specification satisfies *both*.

As indicated in the last response, the issue with respect to the first criterion in this application is thus whether one of ordinary skill in the art can (a) make a protein variant that has 90% sequence identity to SEQ ID NOs:2, 4, 6, 8 or 10 using *routine* methods, and (b) determine whether such variants have microtubule-stimulated ATPase activity using *routine* methods. Applicants submit that the answer to both of these inquiries is "yes."

With respect to issue (a), the application lists a number of references that discuss conventional methods for altering the sequence of proteins (see, e.g., paragraphs [0035] and [0076]-[0079]). The section from the Creighton reference ("Protein Structure: A Practical Approach" (Creighton, T.E., Ed.) IRL Press, 1989, pp. 184-185) provided with the last response also clearly indicates that variants could be made using routine methods, stating "[p]resent day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions." With respect to issue (b), the specification describes a variety of assays that can be routinely utilized to assay for microtubule-stimulated ATPase activity (see, e.g., paragraphs [00135] and [00137] and [00138]).

One of ordinary skill in the art could thus have made variant proteins that have 90% sequence identity with SEQ ID NOs:2, 4, 6, 8 and 10 using techniques that were *routine* in the art. The proteins could then have been *routinely* analyzed for microtubule-stimulated ATPase activity using any of the assays recited in the application. This is all that the law requires to satisfy the requirements of criterion (1) listed above.

Although this is sufficient to demonstrate that the current claims are enabled, the specification also satisfies criterion (2), because the specification provides guidance on the direction that experimentation should proceed to obtain proteins with the recited sequence and activity characteristics. As pointed out in the last response, the specification teaches that the claimed PfKinI-1 proteins are members of the KinI subfamily that is part of the larger kinesin family of proteins (see, e.g., paragraph [0004]), that the PfKinI-1 proteins are homologous with HsKinI-3 (see, e.g., paragraph [0065]), and that some PfKinI-1 proteins include a motor domain, which is a common feature of the kinesin family of proteins (see, e.g., paragraph [0068]). Those

of ordinary skill in the art would thus know that one logical approach for obtaining active variants of SEQ ID NOs:2, 4, 6, 8 and 10 that have microtubule-stimulated activity would involve first identifying conserved and non-conserved regions between the listed protein sequences and related members of the KinI family. This could be readily done using sequence comparison algorithms such as those listed in the specification (see, e.g., paragraphs [0029]-[0031]). Skilled practitioners would further recognize that likely candidates for alteration that would still yield an active protein would be those amino acids in non-conserved regions, as such regions by definition appear to tolerate differences in sequence. Another useful strategy would be to make mutations outside the motor domain because of its role in the activity of the protein. It is thus submitted that the guidance in the specification coupled with the general knowledge in the art would have enabled one of ordinary skill to identify appropriate residues for modification.

The Office Action counters by stating that such comparisons are not helpful because parasites are known to change their antigenicity during the life cycle. This argument has no relevance absent evidence demonstrating that the claimed proteins are cell surface proteins, evidence that the Office has not provided.

Apart from the fact that it appears that the Office Action applies the wrong standard for evaluating enablement, the conclusion the Office Action reaches is at odds with the discussion in the "Synopsis of Application of Written Description Guidelines" (Guidelines) that the Patent Office has promulgated. Applicants recognize that the current rejection is an enablement rather than written description rejection, but the Guidelines nonetheless are pertinent to the current rejection.

As noted in the last response, Example 14 in the Guidelines focuses on a claim example that is similar to the pending claims. The claim reads:

"A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A to B."

In the Analysis section of Example 14, the Office notes that "procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and *retain its activity* are conventional

in the art." (Guidelines, Example 14, emphasis added). This statement thus indicates that the Office has taken the view that those skilled in the art can make active variants that: (i) have a relatively high level of sequence identity to a reference sequence, and (ii) share a specific activity. The proteins that are currently claimed are defined in this manner. Consequently, by analogy to this example, it follows that one of ordinary skill in the art could have made the currently claimed proteins that retained the desired ATPase activity.

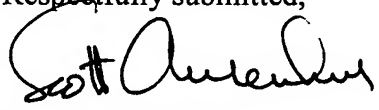
For all the foregoing reasons, it is submitted that the current claims are enabled. Accordingly, it is requested that the enablement rejection be withdrawn.

III. Rejoinder

If the enablement rejection is withdrawn and the claims allowed, Applicants reiterate their request for rejoinder of claims 17 and 18 (see earlier request in response to restriction requirement mailed September 19, 2003. These two claims include all the limitations of claim 8 and thus should be patentable for at least the same reasons as the current claims. The Office in the first Office Action indicated that it would rejoin these claims once the claims currently under examination were allowed.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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